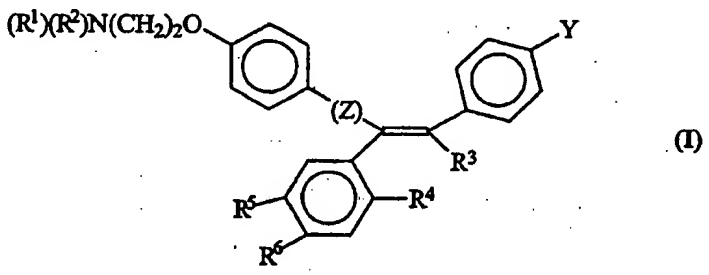
AMENDMENTS TO THE CLAIMS

The listing of claims provided below will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1-172. (Canceled)

173. (Currently amended) A therapeutic method for ~~preventing or~~ treating a cardiovascular or vascular indication characterized by a decreased lumen diameter comprising administering to a mammal at risk of or afflicted with said cardiovascular or vascular indication, a cytostatic dose of a therapeutic agent, wherein the therapeutic agent is a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1.C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

174. (Previously presented) The method of claim 173 wherein the cytostatic dose is effective to increase the level of TGF-beta so as to decrease lesion formation or development, inhibit lipid accumulation, increase plaque stability, maintain or increase vessel lumen diameter, or any combination thereof.

175. (Previously presented) The method of claim 173 wherein the compound of formula (I) is idoxifene, 4-iodotamoxifen, 3-iodotamoxifen, toremifene, or a pharmaceutically acceptable salt thereof.

176. (Previously presented) The method of claim 173 wherein the compound of formula (I) is idoxifene or a pharmaceutically acceptable salt thereof.

177. (Previously presented) The method of claim 173 wherein the compound of formula (I) is toremifene or a pharmaceutically acceptable salt thereof.

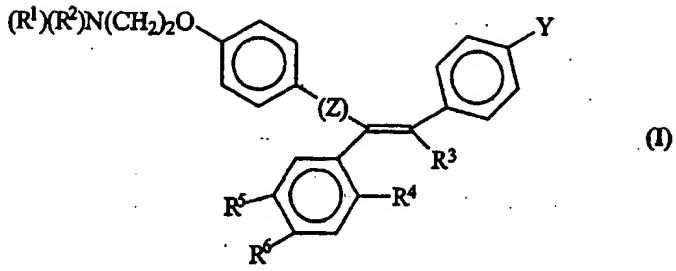
178. (Previously presented) The method of claim 173 wherein the administration is systemic.

179. (Previously presented) The method of claim 173 wherein the compound of formula (I) is administered via a sustained release dosage form.

180. (Previously presented) The method of claim 173 wherein the administration is localized at the site of the vascular trauma.

181. (Previously presented) The method of claim 173 wherein the compound directly or indirectly increases the level of active TGF-beta.

182. (Previously presented) A therapeutic method of increasing the level of TGF-beta in a mammal in need thereof, comprising administering an effective amount of a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyI, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H or together with R^3 is -CH_2-CH_2- or -S-, R5 is I, OH, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

183. (Previously presented) The method of claim 182 wherein the increase in TGF-beta reduces or inhibits diabetic retinopathy.

184. (Previously presented) The method of claim 182 wherein the mammal is diabetic.

185. (Previously presented) The method of claim 184 wherein the diabetic has retinopathy.

186. (Previously presented) The method of claim 182 wherein the compound indirectly or directly increases the level of active TGF-beta in vascular tissue.

187. (Previously presented) The method of claim 182 wherein the compound is a TGF-beta production stimulator.

188. (Previously presented) The method of claim 182 wherein the compound is a TGF-beta activator.

189. (Previously presented) The method of claim 182 wherein the compound increases the production of TGF-beta mRNA.

190. (Previously presented) The method of claim 182 wherein the compound increases the cleavage of the latent form of TGF-beta.

191. (Previously presented) The method of claim 182 wherein the compound increases the bioavailability of TGF-beta.

192. (Previously presented) The method of claim 182 wherein the compound is idoxifene or a pharmaceutically acceptable salt thereof.

193. (Previously presented) The method of claim 182 wherein the compound is toremifene or a pharmaceutically acceptable salt thereof.

194. (Previously presented) The method of claim 182 wherein the compound is droloxifene or a pharmaceutically acceptable salt thereof.

195. (Canceled)

196. (Previously presented) The method of claim 173 or 182 wherein the compound forms cellular DNA adducts at level which is reduced relative to DNA adduct formation by tamoxifen.

197. (Previously presented) The method of claim 173 or 182 wherein the compound has estrogenic activity which is reduced relative to the estrogenic activity of tamoxifen.

198. (Previously presented) The method of claim 173 or 182 wherein the compound does not form cellular DNA adducts.

199. (Previously presented) The method of claim 173 or 182 wherein the compound has no estrogenic activity.

200. (Previously presented) A method of increasing the level of TGF-beta in a mammal in need thereof, comprising administering an effective amount of an agent that directly or indirectly elevates the level of active TGF-beta in said mammal, wherein the agent has reduced estrogenic activity relative to tamoxifen, reduced DNA adduct formation relative to tamoxifen, or any combination thereof.

201. (Previously presented) The method of claim 200 wherein the agent is a structural analog oftamoxifen or a pharmaceutically acceptable salt thereof.

202. (Previously presented) The method of claim 200 wherein the agent is idoxifene or a pharmaceutically acceptable salt thereof.

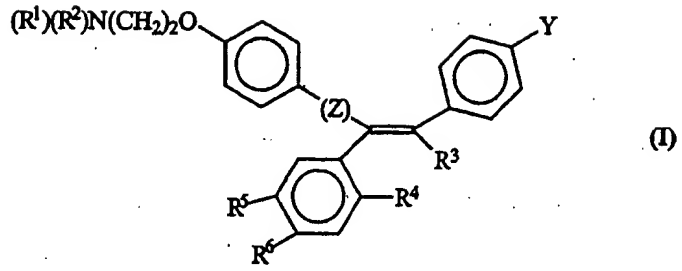
203. (Previously presented) The method of claim 200 wherein the agent is toremifene or a pharmaceutically acceptable salt thereof.

204. (Canceled)

205. (Previously presented) The method of claim 173, 182, or 200 wherein the administration increases the level of latent TGF -beta relative to the level of latent TGF -beta prior to said administration.

206. (Previously presented) The method of claim 173, 182, or 200 wherein the administration increases the level of active TGF -beta relative to the level of active TGF-beta prior to said administration.

207. (Currently amended) A therapeutic method for ~~preventing or~~ treating a vascular indication characterized by a decreased lumen diameter comprising administering to a mammal at risk of or afflicted with said vascular indication, a cytostatic dose of a therapeutic agent, wherein the therapeutic agent is a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H or together with R^3 is -CH_2-CH_2-or-S-, R^5 is I, OH, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

208. (Previously presented) The method of claim 207 wherein the cytostatic dose is effective to increase the level of TGF-beta so as to decrease lesion formation or development, inhibit lipid accumulation, increase plaque stability, maintain or increase vessel lumen diameter, or any combination thereof.

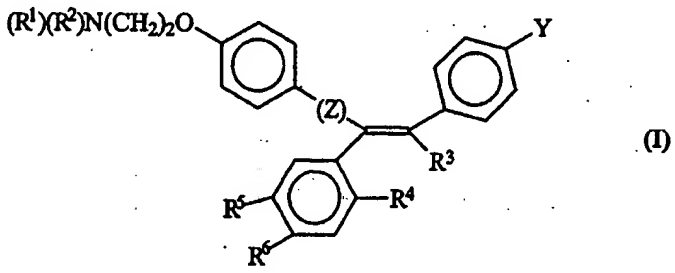
209. (Previously presented) The method of claim 207 wherein the compound of formula (I) is idoxifene, 4-iodotamoxifen, 3-iodotamoxifen, toremifene, or a pharmaceutically acceptable salt thereof.

210. (Previously presented) The method of claim 207 wherein the administration is systemic.

211. (Previously presented) The method of claim 207 wherein the compound of formula (I) is administered in a sustained release dosage form.

212-230. (Canceled)

231. (Previously presented) A therapeutic method for treating a condition selected from the group consisting of arteriosclerosis and small vessel disease, comprising administering to a mammal afflicted with said condition, an effective amount of a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or Hand R^6 is I, O(C_1C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

232. (Canceled).